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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,135	09/08/2000	Kazuko Hirabayashi	44342.011800	2368

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/646,135	HIRABAYASHI ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 5/3/04.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 4-11 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 4-11 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/3/04 has been entered.

Claims 4-11 are pending.

Applicants' traversal and the amendment to claims 4 and 5 in paper filed on 5/3/04 is acknowledged and considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 4-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 5 are rejected under 112 second paragraph because the limitation "with reduced toxicity" in the pre-amble is indefinite. The metes and bounds of the limitation is not defined by the claims because the claims do not define reduced toxicity to what.

Claims 6-11 are rejected under 112 second paragraph because the claims depend on claims 4 and 5.

Claim Rejections - 35 USC § 103

In view of the 112 second paragraph rejection and compact prosecution, the limitation "with reduced toxicity" will not have any weight in the prior art rejection.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4, 5, 7, 8, 10, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wooley et al., (American Journal of Veterinary Research, Vol. 35, pp. 267-73, 1974, cited on a prior PTO-892) taken with Yano et al., (YANO 1) (US Patent No. 5,298,614, cited on prior PTO-892) in further view of Yano et al., (YANO 2) (EP 0685457A1, IDS).

Wooley teaches treating infectious canine hepatitis virus in dogs by subcutaneously administering poly I:C to the dogs before infecting the dogs with the virus. Wooley teaches that double stranded polymers of poly I:C have been shown to induce interferon in vitro and in vivo (page 1217). The antiviral activity of poly I:C has been studied in viral infections in man and several animal species. However, Wooley does not specifically teach a method of treating hepatitis in a human using a cationic liposome (e.g. 2-O-(2-diethlaminoethyl)carbamoyl-1,3,-O-dioleoylglcerol and a phospholipid) with poly I:C, which has a mean length within the range of 100 to 500bp.

However, at the time the invention was made, Yano 1 teaches the poly I: poly C is a substance having a significant activity such as interferon induction action (column 3, lines 32-40). Yano further teaches that when the chain length is limited to certain ranges, the resulting substance exhibit desired physiological activity with markedly less toxicity (column 4, lines 31-39). Yano teaches that experimental techniques have been developed for more accurately determining the molecular weight of macromolecular substances using gel electrophoresis (columns 8 line 61- column 9, line 15). Yano teaches that the fact that the control of molecular

size of nucleic acid polymer within a specified range is the primarily important factor for remarkable reduction of toxicity of poly I: poly C and the preferred molecular size for using poly I: poly C is from 100 to 600 base numbers (column 11, lines 13-34). Yano further teaches different types of delivery: subcutaneous, intramuscular, or intravenous (column 18, line 32-46).

In addition, Yano 2 teaches using a complex (2-O-(2-diethlaminoethyl)carbamoyl-1,3,-O-dioleoylglcerol and a phospholipids, e.g., phosphatidylcholine) to administer double stranded RNA to an individual and that using the lipid reduces toxicity of the double stranded RNA and improves the uptake efficiency of the double stranded RNA into cells ('457, abstract and pages 2-11).

At the time the invention was made it would have been *prima facie* obvious for a person of ordinary skill to use 2-O-(2-diethlaminoethyl)carbamoyl-1,3,-O-dioleoylglcerol and a phospholipid with poly I:C, wherein the poly IC has a mean length within the range of 100 to 500 bp to treat a hepatitis virus in humans. One of ordinary skill in the art would have been motivated to use 2-O-(2-diethlaminoethyl)carbamoyl-1,3,-O-dioleoylglcerol and a phospholipid with poly I:C for treating hepatitis in a human because the lipid reduces toxicity of the double stranded RNA and improves the uptake efficiency of the double stranded RNA into cells of a mammal.

In addition, at the time the invention was made it would have been *prima facie* obvious for a person of ordinary skill to use the complex taught by Yano 1 and Yano 2 for administering poly I:C, which has a mean length within the range of 100 to 500 bp to treat hepatitis in a human. One of ordinary skill in the art would have been motivated to use poly I:C, which has a mean

length within the range of 100 to 500bp in the method because this range displays reduce toxicity of the double stranded RNA in a mammal.

In addition, at the time the invention was made it would have been *prima facie* obvious for a person of ordinary skill to use the complex taught by Yano 1 and Yano 2 for administering poly I:C, which has a mean length within the range of 100 to 500 bp to treat hepatitis in a human. One of ordinary skill in the art would have been motivated to use the complex taught by Yano 1 and Yano 2 with poly I:C for treating hepatitis in a human because Wooley teaches treating canine hepatitis virus in dogs and that poly I:C has anti-viral activity and hepatitis is a viral infection.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 4, 5, 6, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wooley et al., (American Journal of Veterinary Research, Vol. 35, pp. 267-73, 1974, cited on a prior PTO-892) taken with Yano et al., (YANO 1) (US Patent No. 5,298,614, cited on prior PTO-892) and Yano et al., (YANO 2) (EP 0685457A1, IDS) in further view of Liaw (J. Gastroenterol. Hepatol. 1997, 12:S346-53).

The rejection of the base claims 4 and 5 under 35 U.S.C. 103(a) is applied here as indicated above by Wooley et al., taken with (YANO 1) and (YANO 2). However, Wooley et al., taken with (YANO 1) and (YANO 2) do not teach using the complex to treat hepatitis C in a human.

However, at the time the invention was made, Liaw teaches that interferon (IFN) is the only approved and widely used agent for the treatment of HBV, HCV, and HDV (page S346).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wooley et al., taken with (YANO 1) and (YANO 2) in further view of Liaw, namely to use the complex to treat hepatitis C in a human. One of ordinary skill in the art would have been motivated to use the complex to treat hepatitis C in a human because the complex is known to induce interferon in a mammal and interferon is known to treat HCV.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Conclusion

US 4,140,761 is cited on the PTO-892 because the '761 patent could be used as the primary reference instead of Wooley in the 103(a) rejections in the instant office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, SPE - Art Unit 1635, can be reached at (571) 272-0760.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal

Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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